WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 7, 800-806. Review Article ISSN 2277– 7105

KUNDRU (RESIN OF *BOSWELLIA SERRATA ROXB.)*, A LEUKOTRIENE INHIBITOR AND A HERB OF FUTURE

Sharma Anil*[1], Sharma Shamma[2] and Sharma Kumar Dharminder[3]

*[1]Assistant Professor, P.G. Dept. of Swasthavritta and Yoga, Govt. Ayurvedic Medical College Akhnoor, Jammu and Kashmir, UT.

[2]Assistant Professor, P.G. Dept. of Dravyaguna, Govt. Ayurvedic Medical College Akhnoor, Jammu and Kashmir, UT.

[3]Assistant Professor, P.G. Dept. of Rasa-Shastra Evam Bhaishajya Kalpana, Govt. Ayurvedic Medical College Akhnoor, Jammu and Kashmir, UT.

Article Received on
03 May 2020,

Revised on 23 May 2020,
Accepted on 12 June 2020,

DOI: 10.20959/wjpr20207-17868

***Corresponding Author**
Dr. Sharma Anil
Assistant Professor, P.G. Dept. of Swasthavritta and Yoga, Govt. Ayurvedic Medical College Akhnoor, Jammu and Kashmir, UT.

ABSTRACT

Corona virus disease (COVID-19) is caused by SARS-COV2 and represents the causative agent of a potentially fatal disease that is of great global public health concern. Corona virus is one of the major pathogens that primarily targets the human respiratory and immune system. In this review, this article aims to hypothise probable effect of herbal medicine namely Kundru (*Boswellia serrata Roxb.-Resin*) in modulating inflammation and immune response in covid-19 infection and future suggestions in this regard**.**

KEYWORDS: Kundru (*Boswellia serrata Roxb. Resin*)

INTRODUCTION

Since starting of 2020, the world has been struggling in controlling the *Novel* 2019 coronavirus *SARS-CoV-2* (*COVID-19) pandemic that originated in* Wuhan, Hubei Province, China in December 2019. This is due to the lack of immunity in the general population against this novel pathogen and poor understanding of disease pathogenesis and hence no effective treatment till date. Of the various drugs being explored, only *Remdesivir* has been issued an Emergency Use Authorization in the U.S. for those hospitalized with severe disease but again is not an exact treatment.

The first group of patients in China was labeled as suffering from pneumonia of an unknown etiology. The incubation period of COVID-19 infection varies between 5-14 days. It may be shorter among elderly patients and those with suppressed immune system. The most common symptoms are fever, cough, fatigue, sputum production, headache, haemoptysis, diarrhoea and breathlessness. In contrast to the earlier SARS-CoV infection in 2003, COVID19 patients experience higher frequency of gastrointestinal upset, abnormal respiratory findings and increased levels of plasma pro-inflammatory cytokines.

In some cases, the multiple peripheral ground-glass opacities were observed in subpleural regions of both lungs that likely induced both systemic and localized immune response that led to increased inflammation.[1]

In Ayurveda, Inflammation is known by different names in different contexts namely Shotha, Shopha, Svayatu, Utsedha. Ayurveda describes the concept of inflammation as (a) symptom of a disease (b) an independent disease and (c) a complication of diseases. Acharya Charak has mentioned diseases like Kasa (cough), Shwas (Dyspnoea), Jwara (Fever), Atisaar (Diarrhoea) etc. as aetiology of endogenous inflammation and the same along with Aruchi (anorexia), Trishna (thirst), Daurbalya (general weakness) are described in complications of Shotha.[2] The same are also observed as symptoms of Covid-19 infection.

In Ayurveda, Acharya charak has quoted in the chapter of Janapadodhwans that people also get destroyed by raksasa (germ) and varieties of other creatures due to sinful and such other acts.[3] But in the verse term Raksasa and Bhoota might be used to denote bacteria or viruses. The chapter Janapadodhwans denotes to epidemics and when epidemic spreads over multiple countries or continents then it is called pandemic. Janapadodhwans occurs due to vitiation of vayu, jala, desh, kala. They are nothing but modes by which infectious diseases spread and this spread might easily involve large population, due to unhygienic conditions and low immunological status of individual. In kushth nidaan Acharya sushruta has also described Aupasargik rogas i.e. contagious diseases which spread through direct contact or contact with contaminated objects of patients.[4]

Role of the immune system and cytokine storm in COVID19 infection

The main pathogenesis of COVID-19 infection is an altered immune system and inflammatory response. Significantly high blood levels of cytokines and chemokines were noted in patients with COVID-19 infection. The levels are even higher in patients with severe

disease admitted in intensive care units. This exaggerated release of inflammatory mediators is termed as ***Cytokine Storm***. These patients show high levels of IL1-β, IL1RA, IL7, IL8, IL9, IL10, basic Fibroblast Growth Factor-2, granulocyte colony-stimulating factor (G-CSF), GMCSF, IFN-γ, IP10, MCP1, macrophage inflammatory protein 1α (MIP1α), MIP1β, PDGFB, tumour necrosis factor (TNF), and vascular endothelial growth factor (VEGFA). Although release of these cytokines is meant as a disease-fighting response of body against external pathogens, an exaggerated release proves detrimental to body with symptoms of sepsis that are the cause of death in upto one-third to one-fourth of fatal COVID-19 cases. Cytokine storm and the uncontrolled inflammation leads to multi-organ dysfunction, especially of the cardiac, hepatic and renal systems. Unrestricted inflammatory cell infiltration can mediate damage in the lung through excessive secretion of proteases and reactive oxygen species, in addition to the direct damage resulting from the virus. Older people and people with co-morbidities are more likely to develop such a dysfunctional immune response that causes pathology and also fails to successfully eradicate the pathogen.

Boswellia serrata, commonly known as Frankincense, is a herb with significant pharmacological activities related to different systems, mentioned in ayurvedic system of medicine. Extracts from the gum resin of Boswellia serrata and some of its constituents including boswellic acids (BA) affect the immune system in different ways. Among the various boswellic acids, 11-keto-beta-boswellic acid (KBA) and acetyl-11-keto-beta-boswellic acid have been observed to be active. It is reported to be useful in the treatment of bronchitis, asthma, cough, bad throat and various GIT problems. It acts as both internal and external stimulant, expectorant, diaphoretic, diuretic and stomachic. The gum is also prescribed in cases of jaundice, diarrhea, dysentery, dyspepsia and hemorrhoids. It is also recommended in weak and unhealthy kind of ulceration.[5]

In Ayurveda, *Boswellia serrata* extract is named as Kundru and known to possess pharmacological properties as.

- Kundru is sweet, bitter, penetrating, good for the skin, pungent after digestion, cures fever, (excess of), perspiration, disease caused by evil-spirits, disease of mouth, Kapha and Vata.[6]
- Acharya Sushruta described Kundru in Eladi group and the herbs placed in this group pacifies vata and kapha, destroys poison, improves complexion, relieves itching, boils and allergic eruptions.[7]

Boswellia serrata is useful in ailments such as diarrhea, asthma, arthritis, inflammation of viscera, skin diseases, ulcers, chronic bronchitis, depression, hematemesis or bleeding from any part of the body. In afore mentioned disorders, this herb has been pharmacologically and clinically proven as it has anti-arthritic, anti-diarrheal, anti-depressant, anti-asthmatic, anti-inflammatory, anti-convulsant properties and useful in inflammatory bowel diseases. Moreover, recently the other pharmacological activities such as anti-cancer, hepato-protective, hypolipidemic, and hypoglycemic properties are also confirmed. These activities are credited to its phyto-chemical constituents such as boswellic acid, tannin, phenol, β-sitosterol, etc.[8]

Pharmacological Activities

1. Antiviral activity

Researches have been carried out which proves antiviral (against RNA viruses) activity of boswellia.

- One hundred fifty two methanol and water extracts of different parts of 71 plants commonly used in Sudanese traditional medicine were screened for their inhibitory effects on hepatitis C virus (HCV) protease (PR) using *in vitro* assay methods. Thirty four extracts showed significant inhibitory activity. Of these, eight extracts were the most active and methanol extracts of *Boswellia carterii was one of them.*[9]
- Traditional medicines (having anti-viral effects) namely curcumin and *Boswellia serrata* gum resin extract were examined for antiviral activity against CHIKV. Both compounds blocked entry of CHIKV Env-pseudotyped lentiviral vectors and inhibited CHIKV infection in vitro. In addition, vesicular stomatitis virus vector particles and viral infections were also inhibited to the same extent, indicating a broad antiviral activity.[10]

2. Anti-inflammatory Activity on New Papaya Latex Model

- The Boswellic acid from *B. serrata* when tested on new model i.e Papaya Latex Model, showed significant activity of mean 35% inhibition of inflammation. Since the new model is reported to be sensitive to slowly acting, remission inducing drugs. Its effectiveness on boswellic acid throws some light on its mechanism of action which seems to be unlike aspirin and steroidal drugs.[5]

- Leukotriene Inhibition

Ethanol extract of the gum resin inhibits the formation of Leukotriene B4 in rat peritoneal neurophils. Leukotriene such as LTB4 is recognized as one of the important mediators of inflammatory reactions. Leukotrienes are synthesized by stimulated phagocytes cells, particularly the neutrophills. The production of chemostatic factors by these cells attracts more phagocytes to sites of inflammation. Most other non-steroidal anti-inflammatory drugs act through the inhibition of prostaglandins produced by stimulated phagocytes. Boswellic acid, therefore, is different from other known non-steroidal anti-inflammatory drugs in its mode of action and relatively free from side effects.[5]

It inhibits an inflammatory pathway driven by an enzyme called 5-lipoxygenase, (5-LOX). In patients with asthma, boswellic acid (BA) has been found to improve pulmonary function, reduce asthma attack frequency and decrease inhaler usage. BAs increase phagocytosis of macrophages and inhibit activation of NF kappa-B inflammatory pathway. This leads to a reduction of proinflammatory mediators mentioned above such as IL-1, IL-2, IL-4, IL-6 and IFN-gamma. It also inhibits the conversion of C3 into C3a and C3b, and thus classic way of the complement system. In diabetes, 11-keto-ß-boswellic acids act via interference with the NF kappa-B inflammatory pathway to decrease inflammation. *Boswellia* extracts have been shown to decrease injury to micro-vascular endothelial cells by preventing TNFα-induced expression. The anti-inflammatory effect of *Boswellia* extracts is not strictly dependent on the presence of BAs, but it can be related to other bioactive molecules such as the triterpenes, polysaccharides etc.

3. Immunomodulatory activity

Extract of gum resin of B. serrata containing 60% acetyl 11-keto beta boswellic acid (AKBA) along with other constituents such as 11-keto beta-boswellic acid (KBA), acetyl beta-boswellic acid and beta-boswellic acid has been evaluated for antianaphylactic and mast cell stabilizing activity using passive paw anaphylaxis and compound 48/80 induced degranulation of mast cell methods. The extract inhibited the passive paw anaphylaxis reaction in rats in dose-dependant manner. However, the standard dexamethasone (0.27 mg/kg, p.o) revealed maximum inhibition of edema as compared to the extract. A significant inhibition in the compound 48/80 induced degranulation of mast cells in dose-dependant manner was observed thus showing mast cell stabilizing activity. The standard disodium

cromoglycate (50 mg/kg, ip) was found to demonstrate maximum per cent protection against degranulation as compared to the extract containing 60% AKBA.

4. Antidiarrhoeal

Boswellia serrata extract (BSE) was found effective in treating diarrhoea in patient with inflammatory bowel syndrome without causing constipation. It was also found effective against acetylcholine and barium chloride induced diarrhoea by inhibiting contraction of intestinal smooth muscles. The extract also inhibited gastrointestinal transit in croton and castor oil induced diarrhoea in mice. However, intestinal motility remained unaffected in control mice by BSE.[5]

5. Anti-asthmatic activity

In a double blind placebo control clinical study use encapsulated powdered gum resin of Boswellia serrata (S-compound^{TM}, Rahul pharma jammu tawi, India) with 300 mg thrice daily dose for 6 weeks, Gupta et al (1998) established anti-asthmatic potential of gum resin of Boswellia serrata where 70% of the patients with prolong history of asthma showed improvement in physical symptom and sign of dyspnoea, bronchi, number of attacks.[11]

Concluding, with above mentioned pharmacological actions, *Boswellia serrata* may be effective as an adjuvant therapy in the management of COVID 19 patients as it has been proved to be effective as an antiviral agent (RNA virus induced diseases) and also shown activity in symptoms associated with the latter.

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